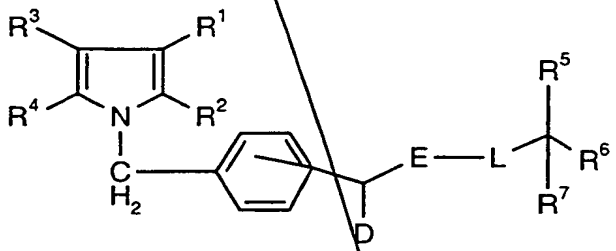
Patent Claims

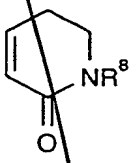
1. Use of a combination of at least one MTP inhibitor as component A of the general formula (A1)



(A1)

in which

R^1 and R^2, including the double bond connecting them, together form a phenyl or pyridyl ring or a ring of the formula



in which

R^8 denotes hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

R^3 and R^4, including the double bond connecting them, together form a phenyl ring or a 4- to 8-membered cycloalkene or oxocycloalkene radical,

all ring systems mentioned under R^1/R^2 and R^3/R^4 optionally being substituted up to 3 times, identically or differently, by halogen, trifluoromethyl, carboxyl, hydroxyl, by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or by

straight-chain or branched alkyl having up to 6 carbon atoms, which for its part can be substituted by hydroxyl or by straight-chain or branched alkoxy having up to 4 carbon atoms,

D represents hydrogen, cycloalkyl having 4 to 12 carbon atoms or straight-chain or branched alkyl having up to 12 carbon atoms,

E represents the -CO- or -CS- group,

L represents an oxygen or sulphur atom or a group of the formula $-NR^9$,

in which

R^9 denotes hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl or phenyl,

R^5 denotes phenyl or a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O,

the cyclic systems optionally being substituted up to 3 times, identically or differently, by nitro, carboxyl, halogen, cyano or by straight-chain or branched alkenyl or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl, carboxyl or by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

and/or the cyclic systems optionally being substituted by a group of the formula $-OR^{10}$ or $-NR^{11}R^{12}$,

in which

R^{10} denotes hydrogen or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms,

R^{11} and R^{12} are identical or different and denote phenyl, hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms or straight-chain or branched acyl having up to 8 carbon atoms, which is optionally substituted by a group of the formula $-NR^{13}R^{14}$,

in which

R^{13} and R^{14} are identical or different and denote hydrogen or straight-chain or branched acyl having up to 8 carbon atoms,

R^6 represents hydrogen, carboxyl or straight-chain or branched alkoxycarbonyl having up to 5 carbon atoms,
or represents straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl or by a group of the formula $-O-CO-R^{15}$,

in which

R^{15} denotes phenyl which is optionally substituted up to 3 times, identically or differently, by halogen, hydroxyl or by straight-chain or branched alkyl having up to 5 carbon atoms,
or denotes straight-chain or branched alkyl or alkenyl each having up to 22 carbon atoms, each of which is optionally

substituted by a group of the formula -OR^{16},

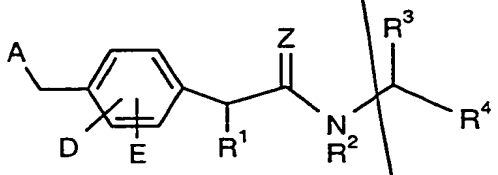
in which

R^{16} denotes hydrogen, benzyl, triphenylmethyl or straight-chain or branched acyl having up to 6 carbon atoms,

R^7 represents hydrogen or

R^6 and R^7 together represent the group of the formula =O,

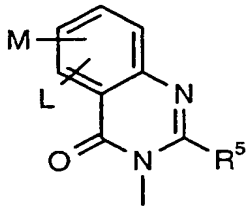
or of the general formula (A2)



(A2)

in which

A represents a radical of the formula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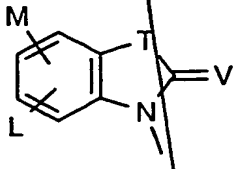
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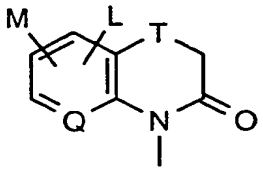
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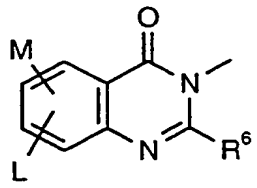
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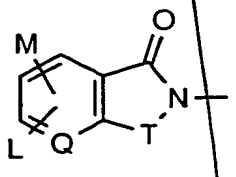
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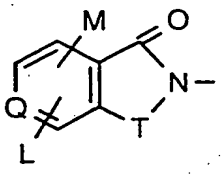
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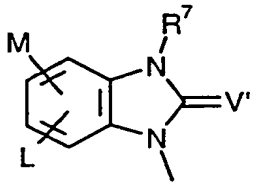
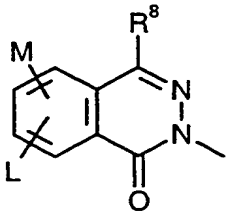
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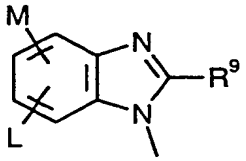


in which

L and M are identical or different and

denote hydrogen, halogen, trifluoromethyl, carboxyl, cycloalkyl having 3 to 6 carbon atoms, hydroxyl, phenyl or straight-chain or branched alkyl, alkoxycarbonyl or alkoxy each having up to 6 carbon atoms,

Q denotes a nitrogen atom or the -CH- group,

T denotes a group of the formula $-SO_2$ or -CO or an oxygen or sulphur atom,

V denotes an oxygen or sulphur atom,

R^5, R^6, R^7 and R^8 are identical or different and

denote hydrogen, or straight-chain or branched alkyl having up to 6 carbon atoms, benzyl or phenyl, each of which is optionally substituted by halogen or by straight-chain or branched alkyl having up to 6 carbon atoms,

R^9 denotes trifluoromethyl, benzyl or a 5- to 7-membered, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, which is optionally substituted up to 3 times, identically or differently, by halogen,

phenyl, hydroxyl or by straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms, or
denotes a group of the formula $-S(O)_a-R^{10}$,

in which

a denotes a number 0, 1 or 2,

R^{10} denotes straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by straight-chain or branched acyl having up to 6 carbon atoms or by aryl or aroyl each having up to 10 carbon atoms, which for their part can be substituted up to 2 times, identically or differently, by halogen, trifluoromethyl or by straight-chain or branched acyl having up to 5 carbon atoms, or
denotes aryl having 6 to 10 carbon atoms, which is optionally substituted by halogen, hydroxyl, trifluoromethyl or straight-chain or branched alkyl or alkoxy each having up to 5 carbon atoms,

D and E are identical or different and
represent hydrogen, halogen, trifluoromethyl, hydroxyl, carboxyl or straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

Z represents an oxygen or sulphur atom,

R^1 represents cycloalkyl having 3 to 10 carbon atoms or
straight-chain or branched alkyl having 1 to 10 carbon atoms, or
represents phenyl which is optionally substituted up to 2 times,

identically or differently, by halogen, nitro, cyano, hydroxyl, straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

R^2 represents hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

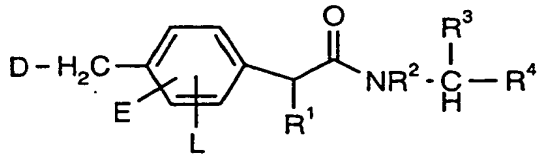
R^3 represents hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms, or
represents cycloalkyl having 3 to 7 carbon atoms, or
represents phenyl or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, each of which is optionally substituted up to 3 times, identically or differently, by halogen, nitro, phenyl, hydroxyl or by straight-chain or branched alkyl or alkoxy having up to 6 carbon atoms,

R^4 represents hydrogen or a group of the formula $-CH_2-OH$ or $CH_2O-CO-R^{11}$,

in which

R^{11} denotes hydrogen, straight-chain or branched alkyl having up to 8 carbon atoms or phenyl which is optionally substituted up to 3 times, identically or differently, by halogen, hydroxyl, cyano or straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

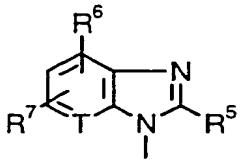
or of the general formula (A3)



(A3)

in which

D represents a radical of the formula



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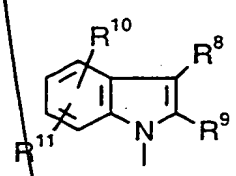


in which

T denotes a nitrogen atom or the -CH- group,

R^6, R^7, R^{10} and R^{11} are identical or different and

denote hydrogen, trifluoromethyl, halogen or straight-chain or branched alkyl or alkoxy each having up to 6 carbon atoms,

R^5, R^8 and R^9 are identical or different and

denote hydrogen, cycloalkyl having 3 to 6 carbon atoms, phenyl, straight-chain or branched alkoxycarbonyl having up to 6 carbon atoms or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by halogen,

or, if T represents a nitrogen atom, R^5 can also denote benzyl,

E and L are identical or different and

represent hydrogen, halogen, trifluoromethyl, hydroxyl, carboxyl or straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

R^1 represents cycloalkyl having 3 to 10 carbon atoms or straight-chain or branched alkyl having 1 to 10 carbon atoms, or represents phenyl which is optionally substituted up to 2 times, identically or differently, by halogen, cyano, hydroxyl, straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

R^2 represents hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

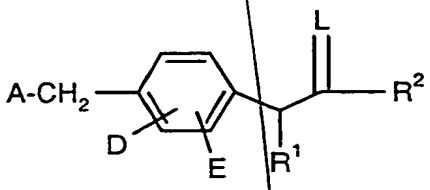
R^3 represents hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms, or
represents cycloalkyl having 3 to 7 carbon atoms, or
represents phenyl or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, each of which is optionally substituted up to 3 times, identically or differently, by halogen, nitro, phenyl, hydroxyl or by straight-chain or branched alkyl or alkoxy having up to 6 carbon atoms,

R^4 represents hydrogen or a group of the formula $-CH_2-OH$ or $CH_2O-CO-R^{12}$,

in which

R^{12} denotes hydrogen, straight-chain or branched alkyl having up to 8 carbon atoms or phenyl which is optionally substituted up to 3 times, identically or differently, by halogen, hydroxyl, cyano or straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

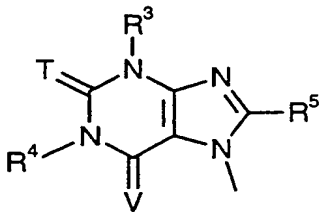
or of the general formula (A4)



(A4)

in which

A represents a radical of the formula



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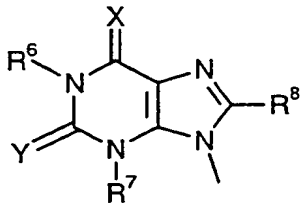


,

in which

R^3, R^4, R^6 and R^7 are identical or different and

denote hydrogen, cycloalkyl having 3 to 7 carbon atoms or aryl having 6 to 10 carbon atoms,

or denote straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by halogen, hydroxyl or aryl having 6 to 10 carbon atoms,

T, V, X and Y are identical or different and denote an oxygen or sulphur atom,

R^5 and R^8 are identical or different and

denote hydrogen, halogen, cycloalkyl having 3 to 8 carbon atoms or straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally

substituted by cycloalkyl having 3 to 8 carbon atoms, or by a 5- to 6-membered, aromatic, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, or by aryl having 6 to 10 carbon atoms, where the cyclic systems for their part can be substituted up to 3 times, identically or differently, by a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, or by phenyl, benzyl, halogen, hydroxyl, carboxyl or by straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms, or denote aryl having 6 to 10 carbon atoms or a 5- to 7-membered aromatic, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, each of which is optionally substituted up to 3 times, identically or differently, by halogen, phenyl, trifluoromethyl, hydroxyl, carboxyl or by straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or by a group of the formula $-(CO)_a-NR^9R^{10}$,

in which

a denotes a number 0 or 1,

R^9 and R^{10} are identical or different and

denote hydrogen, phenyl or straight-chain or branched alkyl or acyl each having up to 5 carbon atoms,

D and E are identical or different and

represent hydrogen, halogen, trifluoromethyl, hydroxyl, carboxyl or straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

R^1 represents hydrogen or cycloalkyl having 3 to 8 carbon atoms, or represents straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by cycloalkyl having 3 to 6 carbon atoms, phenyl or by a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, or

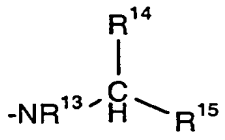
represents phenyl or a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, the ring systems optionally being substituted up to 3 times, identically or differently, by halogen, phenyl, trifluoromethyl or straight-chain or branched alkyl or alkoxy each having up to 5 carbon atoms, hydroxyl or by a group of the formula $-NR^{11}R^{12}$,

in which

R^{11} and R^{12} have the meaning of R^9 and R^{10} indicated above and are identical to or different from this,

L represents an oxygen or sulphur atom,

R^2 represents mercapto, hydroxyl, straight-chain or branched alkoxy having up to 8 carbon atoms or the group of the formula



,

in which

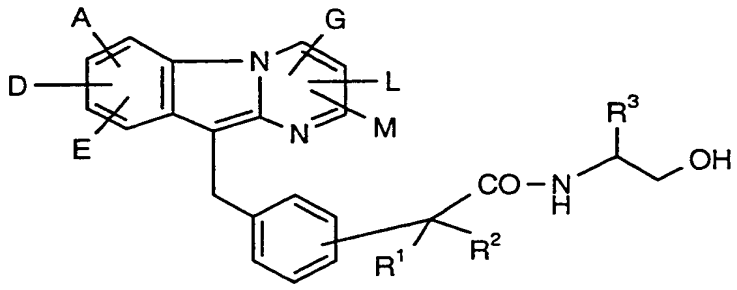
R^{13} denotes hydrogen or straight-chain or branched alkyl having up

to 4 carbon atoms,

R^{14} denotes hydrogen, phenyl or a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O,

R^{15} denotes hydrogen or straight-chain or branched alkyl having up to 8 carbon atoms, which is optionally substituted by hydroxyl,

or of the general formula (A5)



(A5)

in which

A, D, E, G, L and M are identical or different and

represent hydrogen, halogen, trifluoromethyl, carboxyl, hydroxyl, straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or straight-chain or branched alkyl having up to 6 carbon atoms, which for its part can be substituted by hydroxyl or by straight-chain or branched alkoxy having up to 4 carbon atoms,

R^1 and R^2 are identical or different and

represent hydrogen, cycloalkyl having 3 to 8 carbon atoms or straight-chain or branched alkyl having up to 10 carbon atoms, which is optionally substituted by cycloalkyl having 3 to 6 carbon atoms or

represent phenyl which is optionally substituted by halogen or trifluoromethyl, or

R^1 and R^2, together with the carbon atom, form a 4- to 8-membered cycloalkyl ring

and

R^3 represents phenyl which is optionally substituted up to 3 times, identically or differently, by nitro, carboxyl, halogen, cyano or by straight-chain or branched alkenyl or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl, carboxyl or by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,
and/or is optionally substituted by a group of the formula $-OR^4$ or $-NR^5R^6$,

in which

R^4 denotes hydrogen or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms,

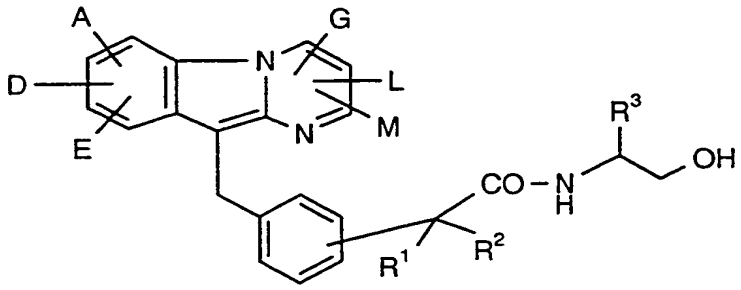
R^5 and R^6 are identical or different and denote phenyl, hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, or denote straight-chain or branched acyl having up to 8 carbon atoms, which is optionally substituted by a group of the formula $-NR^7R^8$,

in which

R^7 and R^8 are identical or different and

denote hydrogen or straight-chain or branched acyl having up to 8 carbon atoms,

or of the general formula (A6)



(A6)

in which

A, D, E, G, L and M are identical or different and

represent hydrogen, halogen, trifluoromethyl, carboxyl, hydroxyl, straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or straight-chain or branched alkyl having up to 6 carbon atoms, which for its part can be substituted by hydroxyl or by straight-chain or branched alkoxy having up to 4 carbon atoms,

R^1 and R^2 are identical or different and

represent hydrogen, cycloalkyl having 3 to 8 carbon atoms or straight-chain or branched alkyl having up to 10 carbon atoms, which is optionally substituted by cycloalkyl having 3 to 6 carbon atoms, or

represent phenyl which is optionally substituted by halogen or trifluoromethyl, or

R^1 and R^2, together with the carbon atom, form a 4- to 8-membered cycloalkyl ring

and

R^3 represents phenyl which is optionally substituted up to 3 times, identically or differently, by nitro, carboxyl, halogen, cyano or by straight-chain or branched alkenyl or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl, carboxyl or by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

and/or is optionally substituted by a group of the formula $-OR^4$ or $-NR^5R^6$,

in which

R^4 denotes hydrogen or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms,

R^5 and R^6 are identical or different and denote phenyl, hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, or denote straight-chain or branched acyl having up to 8 carbon atoms, which is optionally substituted by a group of the formula $-NR^7R^8$,

in which

R^7 and R^8 are identical or different and denote hydrogen or straight-chain or branched acyl having up to 8 carbon atoms,

if appropriate in an isomeric form and their salts

with HMG-CoA reductase inhibitors as component B for the production of medicaments for the prophylaxis and/or treatment of cardiovascular diseases.

2. Use of a combination according to Claim 1 for the production of medicaments for the control or prophylaxis of cardiovascular diseases which are associated with metabolic diseases or deficits.

3. Use of a combination according to Claim 2 for the control of arteriosclerosis, diseases of the coronary vessels of the heart, raised serum lipids, hypercholesterolaemia, hypertriglyceridaemia and mixed forms which are combined with raised VLDL or LDL and/or raised chylomicrons, and of syndrome X.

4. Use of a combination according to Claim 2 for the treatment of secondary hypercholesterolaemia and secondary hypertriglyceridaemia, which are optionally associated with apolipoprotein E polymorphism, obesity, chylomicronaemia and chylomicronaemia syndrome, renal insufficiency, chronic renal insufficiency, nephrotic syndrome, diabetes mellitus type II, and with hepatomas and plasmacytomas.

5. Use of a combination according to Claim 2, characterized in that it contains, as component A, a compound of the general formula (A1).

6. Use of a combination according to Claim 2, characterized in that it contains, as component A, a compound of Examples 1-119.

7. Use of a combination according to Claim 2, characterized in that it contains, as component A, a compound of Examples 92-119.

8. Use of a combination according to Claim 2, characterized in that it contains, as component A, a compound of Examples 48 or 80.

9. Medicament comprising a combination of an MTP inhibitor as component A and an HMG-CoA reductase inhibitor as component B according to Claim 1 and, if appropriate, one or more further suitable components.

10. Medicament according to Claim 9, characterized in that it contains, as component A, the active compound 2-cyclopentyl-2-[4-(2,4-dimethyl-pyrido[2,3-b]indol-9-ylmethyl)-phenyl]-N-(2-hydroxy-1-phenyl-ethyl)-acetamide or 2-cyclopentyl-2-[4-(2,4-dimethyl-pyrimido[1,2-a]indol-10-ylmethyl)-phenyl]-N-(2-hydroxy-1-phenyl-ethyl)-acetamide and, as component B, the active compound atorvastatin, cerivastatin, simvastatin, pravastatin, lovastatin, fluvastatin, itavastatin or ZD 4522.

11. Medicament according to Claim 9, characterized in that it contains, as component A, the compound (2S)-2-cyclopentyl-2-[4-(2,4-dimethyl-pyrido[2,3-b]indol-9-ylmethyl)-phenyl]-N-(2-(1R)-hydroxy-1-phenyl-ethyl)-acetamide.

12. Process for the production of medicaments according to Claim 9, characterized in that the components A and B are converted into a suitable administration form with excipients and vehicles and, if appropriate, with further components.